History

The isolation of morphine by Serturner

Developments in chemistry during the latter part of the 18th century led not only to the synthesis of new drugs but also to the purification of plant extracts used as medicines. These herbal remedies consisted mainly of impure vegetable derivatives containing a number of inert as well as pharmacologically active substances but in unknown quantities and varying proportions. Of the active substances used in medicine around 1800, opium had remained medically important since ancient times.

The isolation of morphine in its pure form was the result of years of research and testing, occurring most prominently between the years 1803 and 1817. Towards the end of the 18th century, a brilliant pharmacist named Friedrich Wilhelm Adam Serturner (1783–1841) transformed pharmaceutical chemistry from a state of alchemy to an acknowledged branch of science.

SERTURNER'S BIOGRAPHY

Born on 19 June 1783, Serturner was the fourth of six children born to Joseph Simon Serdinner and Marie Therese Brockmann in Neuhaus, in North Rhine-Westphalia, Prussia (present-day Austria). His parents were in the service of the Paderborn prince, Friedrich Wilhelm. When the prince and his parents died in 1798, Serturner was left with no means of support. At the tender age of 16, he enrolled as an apprentice to Mr. Cramer, a court apothecary in Paderborn.

THE ISOLATION OF MORPHINE

Through diligent research, Serturner was the first to successfully isolate and extract morphine crystals from the tarry poppy seed juice. After a series of experiments on rats and stray dogs, he reported his discovery of a sleep-inducing molecule in letters to the editor of the Trommsdorffs Journal der Pharmacie in 1805 and again, the following year. Soon after qualifying as an apothecary assistant, Serturner moved to Einbeck in 1806 where he was employed as an assistant in the magistrate's pharmacy. Following Napoleon Bonaparte's invasion into Europe, French legislation prevailed, permitting Serturner, to open shop in Westphalia.[1]

A SEARCH FOR A SAFE DOSE

When his discovery remained unrecognised, Serturner continued with his experiments and described the 'crystallisable' properties of the new substance (*Principium somniferum*) that was a weak base, soluble in acidic solutions. Since his discovery occurred almost 50 years before the invention of the hypodermic syringe, the drug had to be administered orally. Once, in the midst of a terrible toothache, Serturner swallowed a small quantity of his salt and experienced tremendous relief. When he awoke hours later, he realised that this compound was safe for human consumption. By trial and error, through self-administration and dosing three young volunteers, he noticed that one-fourth grain (30 mg) of the drug induced a happy, light-headed sensation, the second dose caused drowsiness and excessive fatigue, while the third caused participants to become confused and somnolent. He suggested that 15 mg of the drug as the optimal dose and named the substance 'Morphium' after the Greek god of sleep and dreams.

A LANDMARK DISCOVERY AND RECOGNITION

Serturner's third publication titled, 'Ueber das Morphium als Hauptbestandteil des Opiums' was well received and recognised by the eminent French Chemist JL Gay-Lussac and also the German Mineralogical Society. The Jena University awarded Serturner an honorary doctor's degree in 1817. He received similar honours from universities at Marburg, Berlin, St. Petersburg, Batavia, Paris and Lisbon. In 1831, Serturner received the Montyon prize from the Institute of France and the title 'Benefactor of Humanity' for his work in isolating morphine from opium.

Serturner had pioneered and promoted a new branch of science that came to be known as alkaloid chemistry. He also disproved the prevailing notion that all medicinal plant substances were acidic in nature. When the term alkaloid was coined in 1818 by W Meissner and the suffix-*ine* applied to the group, morphium came to be known as morphine. When Napoleon was finally defeated, Serturner had to close his pharmacy in Einbeck and establish the 'Rathaus Apotheke' at Hamelin (of Pied Piper fame). His initiative led to the isolation of numerous other alkaloids such as codeine, quinine, strychnine, veratrine and emetine.[2]

A BRILLIANT MIND THAT KNEW FEW BOUNDARIES

Serturner's interests and versatility extended beyond alkaloids is shown by his subsequent studies on the composition of corrosive alkalis and also by his views on the nature of cholera in 1831. He considered the disease to be caused by a living organism that could be eliminated with disinfectants and by boiling drinking water. He then turned his attention to improving the designs of firearms, bullets and other ammunition. He even managed to improve the designs of rear-loaded rifles and created a lead-antimony alloy for making bullets, meriting honours from the Hanoverian government.

Addicted to morphine, Serturner suffered from chronic depression and became severely withdrawn. He died on 20 February, 1841, and was buried in Einbeck.

PAIN CONQUERED

Despite his limited education, Serturner's efforts proved far-reaching. An autodidact, he accomplished his research with only sparse knowledge of the relevant literature and with the simplest equipment. Morphine was not only the first alkaloid to be extracted from opium but also the first ever alkaloid to be isolated from any plant. Serturner's discovery enabled physicians to prescribe morphine in regulated dosages for easing pain and also eliminated the dangers of overdose associated with raw poppy juice, which varied unpredictably in its concentration of morphine from one batch to another. It was only in 1925 that Sir Robert Robinson deduced the empirical formula of morphine and Marshall D. Gates, Jr. synthesised the drug in a laboratory in 1952.[3]

PHARMACOLOGY OF MORPHINE

Morphine sulphate, an opioid agonist, is relatively selective for the mu receptors at sites in the periaqueductal and periventricular grey matter. Morphine can be administered orally, intravenously, rectally, subcutaneously, through spinal injection (e.g. epidural) as well as through inhalation. The principal therapeutic action of morphine is analgesia. Morphine is indicated for the relief of severe acute and severe chronic pain. Other therapeutic effects of morphine include anxiolysis, euphoria and feelings of relaxation. Morphine remains the drug of choice in acute myocardial infarction as it relieves pain and results in significant peripheral vasodilatation and reduction in systemic vascular resistance.[4] The drug is also dramatically effective in cardiogenic pulmonary oedema as it calms the patient and reduces dyspnoea and myocardial oxygen demand.

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